REMARKS:

Claims 1, 30, and 53 are amended. Support for the amendments to claims 1, 30, and 53 can be found on page 8, lines 3-13 of the Applicant's specification. Claims 1-32 and 34-72 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §102:

Claims 1, 3, 7, 9, 11-14, 17-18, 22-28, 53, 55-58, 62, and 66-71 stand rejected under 35 U.S.C. §102(b) as being anticipated by Jahn et al., *Proceedings of the National Academy of Sciences, USA*, (1984), Vol. 81, pages 1684-1687 ("Jahn"). The Applicant respectfully traverses this rejection.

Claim 1, as amended, is as follows:

A method for detecting a target biopolymer in a sample, comprising:

(a) preparing a microarray of said sample by dispensing aliquots of said sample at discrete sites onto a substrate and immobilizing said target biopolymer on said substrate, wherein the microarray is an array of dots, each dot having a diameter from about 1 to 500 microns, wherein each of said aliquots contains the same amount of said target biopolymer;

(b) contacting said microarray with a probe biopolymer under conditions that allow the formation of a complex comprising said target biopolymer and said probe biopolymer; and

(c) detecting the presence of said complex as a measurement for the presence or the amount of the target biopolymer in said sample.

Applicant respectfully submits that Jahn cannot anticipate present claim 1, because Jahn fails to teach preparing a microarray of any sort, much less of

preparing a microarray using the same amounts of sample and then contacting this microarray with a probe to form a complex.

The Examiner, in his Response to Arguments, states that features that the Applicant relies upon such as i) aliquots that are equivalent in composition and concentration and ii) microarrays having dots with a diameter from about 1 to 500 microns are not recited in the rejected claims. In response, the Applicant amended claim 1 to incorporate the diameter of the dot feature in an effort to expedite the prosecution of the application. Consequently, amended claim 1 now recites that the diameter of the dot is from about 1 to 500 microns. However, the Applicant respectfully disagrees with the Examiner's assertion that the "equivalent in composition and concentration feature" is not recited in the claim. Since the microarray is prepared by dispensing aliquots of a sample, the composition and concentration of the aliquots must be the same, because the aliquots come from the same stock. Furthermore, since the aliquots contain the same amount of target, the amount of aliquot added had to have been the same. Consequently, the aliquots as recited in claim 1 are equivalent in composition and concentration.

Jahn is directed to immunoassays using samples spotted on nitrocellulose membranes, not microarrays. Jahn teaches an immunoassay method that provides a parallel handling of a large number of different samples. (Jahn, Abstract). In Jahn, each sample was adjusted to a spotting volume of 20 µl and spotted in three 6- to 7-µl portions on the center of a square, using a hair dryer for drying between the applications. The diameter of the spots was 1.2-1.5 cm. (Jahn, page 1684, column 2, lines 32-35). Accordingly, the spots of Jahn are not the microarrays of the present invention, wherein the diameter of the dot is from about 1 to 500 microns. Additionally, Jahn has no teaching of each spot having the same amount of the analyte. To the contrary, different spots of Jahn contain different samples with different quantities of analyte.

Jahn cannot make instant claim 1 obvious. Jahn has no teaching or suggestion of preparing a microarray using the same amounts of sample and then

contacting this microarray with a probe to form a complex. Jahn discloses a conventional dot-immunobinding assay of proteins in which a large number of different samples are spotted on nitrocellulose membrane filters, incubated sequentially with specific antibodies and ^{125}I-labeled protein A, and assayed for radioactivity. (Jahn, Abstract). Unlike the present invention, Jahn does not utilize a microarray format. Consequently, Jahn's method does not allow for the substantial decrease in an amount of a sample required for testing as described in the present invention. For example, in one embodiment described in the Example 1 on page 18 of the Applicant's specification, only 1 microliter of a sample is required to produce as many as 1000 sample dots locations of a microarray, while a conventional 1536 microtiter plate would require the use of about 2 milliliters per plate. Thus, the present invention offers the advantage that a small amount of sample can be successfully tested with a probe or multiple probes specific for target contained in the sample.

The Examiner states that Jahn and Shuber inherently make some duplicates and this then teaches preparing a microarray of the same sample. The Applicant respectfully disagrees with this reasoning. Preparing one or even many duplicate samples is different than preparing a microarray, wherein all the samples are the same.

In light of the foregoing, Applicant respectfully submits that Jahn could not have anticipated or rendered obvious claim 1, because Jahn fails to teach or suggest each and every claim limitation. Claims 3, 7, 9, 11-14, 17-18, and 22-28 depend from claim 1 and cannot be anticipated or rendered obvious for at least the same reasons as claim 1. Withdrawal of these rejections is thus respectfully requested.

Claim 53, as amended, is as follows:

A method for identifying one or more target analytes in a sample, comprising:

(a) preparing a microarray of said sample by dispensing aliquots of said sample at discrete sites onto a substrate and immobilizing said analytes on said substrate, wherein the microarray is an array of dots, each dot having a diameter from about 1 to 500 microns, wherein each of said aliquots contains the same amount of said target analytes;

(b) contacting said microarray with a plurality of labeled probes specific for each of said target analytes under conditions that allow the formation of a complex between each of said target analytes and said labeled probe specific for said target analyte; and

(c) detecting said complexes as a measurement of the presence or the amount of said target analytes.

Claim 53, although not depending from claim 1, requires the similar limitations of preparing a microarray using equivalent amounts of sample and then contacting this microarray with a plurality of probes to form complexes. Therefore, Jahn could not have anticipated or rendered obvious claim 53 for the same reasons as discussed above. Claims 55-58, 62, and 66-71 depend from claim 53 and cannot be anticipated or rendered obvious for at least the same reasons as claim 53. Withdrawal of these rejections is thus respectfully requested.

Claims 1, 7, 8, 10, 13-14, 17-18, 21-24, 26, 28, 30, 37-40, 44-47, 49, 53, 55-57, 62, 66-68, and 70 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Shuber et al., *Human Molecular Genetics* (1997), Vol. 6(3), pages 337-347 ("Shuber"). The Applicant respectfully traverses this rejection.

Applicant respectfully submits that Shuber cannot anticipate present independent claims 1, 30, and 53 because Shuber, similar to Jahn, fails to teach preparing a microarray of any sort, much less of preparing a microarray using equivalent amounts of sample and then contacting this microarray with a probe or probes to form a complex.

As discussed above, claims 1 and 53 were amended to recite the that the diameter of the dots found in the microarray is from about 1 to 500 microns. Independent claim 30 was similarly amended.

Shuber is directed to a diagnostic assay for analyzing large numbers of different samples (>500) simultaneously for a large number of known mutations. (Shuber, Abstract). Shuber teaches blotting amplified DNA samples, each positive for one of 106 mutations, on a membrane. Shuber utilizes a conventional 96-well dot-blot apparatus and applies 30 µl of sample solution to each well. (Shuber, Figure 3 legend and page 345, column 1 under Dot-blots). A typical size of dots obtained with a 96-well apparatus of the type used by Shuber is a few millimiters in diameter (see, for example, attachment in the Applicant's response of April 23, 2003 to the Office Action dated January 23, 2003). Accordingly, the spots of Shuber are not the microarrays of the present invention, wherein the diameter of the dot is from about 1 to 500 microns. Additionally, Shuber has no teaching of each spot having the same amount of the analyte. To the contrary, different spots of Shuber contain different samples with different quantities of analyte.

Shuber cannot make instant claims 1, 30, and 53 obvious. Shuber, similar to Jahn, has no teaching or suggestion of preparing a microarray using equivalent amounts of sample and then contacting this microarray with a probe to form a complex. Shuber's assay, although different than that of Jahn, is still not a microarray assay. Based on the teachings of Shuber, those skilled in the art would not have recognized that a microarray analysis of a single sample might be successfully performed, where the array is formed by subdividing the single

unknown sample into a microarray of numerous aliquots having an equivalent amount of a target and having a size less than those of Shuber.

In light of the foregoing, Applicant respectfully submits that Shuber could not have anticipated or rendered obvious claims 1, 30, and 53, because Shuber fails to teach or suggest each and every claim limitation. Claims 7, 8, 10, 13-14, 17-18, 21-24, 26, 28, 37-40, 44-47, 49, 55-57, 62, 66-68, and 70 depend from either claim 1, 30, or 53 and therefore, cannot be anticipated or rendered obvious for at least the same reasons as claims 1, 30, and 53. Withdrawal of these rejections is thus respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §103:

Claims 1-19, 21-42, 44-64, and 66-72 stand rejected under 35 U.S.C. § 103(a) over Shuber in view of Balch et al., U.S. Patent 6,312,960 B1 (Balch), November 6, 2001. This rejection is moot with respect to claim 33 due to the Applicant's previous cancellation of this claim in the Applicant's response of April 23, 2003 to the Office Action dated January 23, 2003. With respect to claims 1-19, 21-32, 34-42, 44-64, and 66-72, this rejection is respectfully traversed.

The above claims consist of either independent claims 1, 30, and 53 or claims which depend from them. Consequently, these claims cannot be rendered obvious over Shuber for at least the same reasons as discussed above. Balch cannot remedy the defects of Shuber and is not relied upon by the Examiner for such. Instead, the Examiner cites Balch for teaching features of conventional probe arrays and methods of their making. (Balch, column 4, lines 17-41). Balch neither teaches nor suggests anything related to sample arrays, much less methods of preparing a microarray of a single sample by dispensing aliquots of the sample at discrete sites onto a substrate.

In the probe microarrays of Balch, high concentrations of homogeneous probe solutions are applied to the substrate and reacted with large quantities of sample containing the target. In contrast, in the present invention, as previously noted,

relatively small quantities of sample are immobilized on the substrate and successfully reacted with a solution containing one or several probes.

In light of the foregoing, Applicant respectfully submits that Shuber and Balch could not have made claims 1-19, 21-32, 34-42, 44-64, and 66-72 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Withdrawal of this rejection is thus respectfully requested.

Claims 1-72 stand rejected under 35 U.S.C. § 103(a) over Shuber in view of Balch, further in view of Sirvio et al., U.S. Patent No. 5,532,311 (Sirvio). This rejection is moot with respect to claim 33 due to the Applicant's previous cancellation of this claim in the Applicant's response of April 23, 2003 to the Office Action dated January 23, 2003. With respect to claims 1-32 and 34-72, this rejection is respectfully traversed.

Independent claims 1, 30, and 53 and their dependent claims 2-29, 31, 32, 34-52, and 54-72 are patentable over Shuber and Balch for at least the same reasons as discussed above. Sirvio cannot remedy the defects of Shuber and Balch and is not relied upon by the Examiner for such. Instead, the Examiner cites Sirvio for teaching a substrate being wetted with an organic modifier selected from dextran sulfate or polyacrylic acid. Sirvio provides a general teaching of processes for modifying surfaces. However, Sirvio has no teaching or suggestion whatsoever of methods of making microarrays, much less of methods of preparing sample microarrays.

In light of the foregoing, Applicant respectfully submits that the cited references could not have made claims 1-32 and 34-72 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Withdrawal of this rejection is thus respectfully requested.

Applicant believes the foregoing amendments comply with requirements of form and thus may be admitted under 37 C.F.R. § 1.116(a). In addition, admission is requested under 37 C.F.R. § 1.116(a) as presenting rejected claims in better form for consideration on appeal.

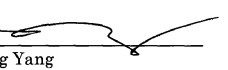
In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

Dated: September 10, 2003

By: 
Wei-Ning Yang
Registration No. 38,690

500 South Grand Avenue
Suite 1900
Los Angeles, California 90071
Telephone: 213-337-6700
Fax: 213-337-6701